

## **REMARKS**

### **Claims Rejections Under 35 USC §103**

Claims 1, 8, 14, 18, 31, 47 and 51 are rejected under 35 USC §103 for reasons previously set forth in the paper mailed from the Office on October 26, 2006, Section 4, page 2 - 5.

Applicant traverses the continuing rejection of the claims because a further review of the US patent # 4,598,089 anti-lipase therapeutic has revealed the following:

The art of U.S. Patent # 4,598,089 recites the oral administration of a leucine derivative, commercially known as Orlistat/Lipstatin or Tetrahydrolipstatin, for the prevention and treatment of obesity by the inhibition of lipase activity. From the New Drug Application (NDA 20-766/S-018) by Roche and its commercial clinical patient information flyer (h:\20766ptlbl.doc) reads the following: "Orlistat is an oral prescription weight loss medication use to help obese people to lose weight and keep this weight off. This product should be used together with a reduced-calorie diet that should contain no more than 30% calories from fat. At a dose of 120 mg three times a day, orlistat inhibits dietary fat absorption by approximate 30%".

Let's assume the following:

A standard daily intake of 2000 calories, 30% of calories supplied from fat, 60% from carbohydrates and 10% from protein (from FDA Daily Values).

### Calories and Intake based on FDA daily values

Nutrient	% Calories <sup>1</sup>	Total Calories <sup>2</sup>	Grams Food <sup>3</sup>
Fat	30	600	65
Carbohydrates	60	1200	300
Protein	10	200	50
<b>Total</b>	<b>100</b>	<b>2000</b>	<b>415</b>

<sup>1</sup>Percentage of calories supplied by each nutrient.

<sup>2</sup>Net calories supplied by each nutrient from a 2000 cal diet.

<sup>3</sup>one gram fat=9 calories, gram carbohydrate=4 cal, gram protein=4 cal.

From the table above we can see that fat supplies 600 calories, if Orlistat inhibits 30% of fat then 180 calories ( $600 \times 30\%$ ) will not be absorbed. If 1 gram of fat can supplied 9 calories then the amount of extra fat that someone can eat without gaining any weight will be 20 grams ( $180 / 9$ ). Then the new total intake will be 435 gr or 4.8% more feed (( $435/415 \times 100$ )-100).

Nutrient	% Calories <sup>1</sup>	Total Calories <sup>2</sup>	Grams Food <sup>3</sup>	Grams Food after Orlistat
Fat	30	600	65	85
Carbohydrates	60	1200	300	300
Protein	10	200	50	50
<b>Total</b>	<b>100</b>	<b>2000</b>	<b>415</b>	<b>435</b>

<sup>1</sup>Percentage of calories supplied by each nutrient.

<sup>2</sup>Net calories supplied by each nutrient form a 2000 kcal diet.

<sup>3</sup>gram fat=9 cal, gram carbohydrate=4 cal, gram protein=4 cal.

In summary, a normal person consuming 2000 cal/day and taking orlistat three time a day can eat 20 more grams of fat.

However, when compared with the instantly claimed invention it becomes quite clear that the instant invention is surprisingly superior to the invention of the primary reference recited in the instant rejection.

A control subject needs 2000 cal/day or 415 gr food/day to maintain body weight. The instant invention has demonstrated that a mammal taking the compound of the present invention can eat 35.5% more food than the control and maintain comparable weight as the control (Example 5, from table on Page 9 of application), or if translated into a human subject, it would be expected that the human subject could eat 147.3 gr (415gr x 35.5%) more food a day and have comparable weight to the control subjects.

It is clear that the instant application is not obvious over US Patent # 4,598,089 or US Patent # 4,598,089 in combination with the secondary references (Ohkaru (Clin, Chim. Acta 182:295-300), JP 02150294, US Patent # 5,585,098 and U.S. Patent # 5,080,895). Applicant therefore requests withdrawal of the instant grounds or rejection.



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: JULIO L. PIMENTEL, Ph.D.  
Application #: 08/888,202  
Filed : July 7, 1997  
Group art unit : 1642  
For : "DECREASED FAT ABSORPTION WITH AN ANTI-LIPASE ANTIBODY"

April 24, 2007

**COMMISSIONER FOR PATENTS**

**P.O. Box 1450**  
**Alexandria, VA 22313-1450**

Sir:

I, Julio L. Pimentel Ph.D. declares as follows:

I am the Julio L Pimentel listed as inventor of the above-identified application.

I have a Ph.D. degree in Nutritional Sciences from the University of Wisconsin-Madison. I have been conducting research in the area of avian antibodies since 1984 and I am co-author of several patents related to avian antibodies. I am currently Research and Development Manager at Anitox Corporation in Georgia and freelance researcher at G.V.D. Corp. Experiments conducted in my laboratory have demonstrated the effect of using antibodies against lipase on animal performance as shown in Exhibit A.

I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and, further, that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of

the United States Code and that such willful false statements may jeopardize the validity of the application or document or any patent issuing therefrom.



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## EXHIBIT A

### **Effect of avian anti-lipase antibody on the growth and feed intake of rats.**

#### **Scope**

To determine the usefulness of avian anti-lipase antibodies on the weight gain of rats.

#### **Material and Methods**

**Antigen:** The antigen used for immunization of hens was Lipase from porcine pancreas (Sigma # L-0382), Type VI-S, lyophilized powder with  $\geq 20,000$  units/mg protein. The protein content is 40-60%. One unit hydrolyzes 1.0 microequivalent of fatty acid from a triglyceride in 1 hr at pH 7.7 at  $37^{\circ}\text{C}$  using olive oil.

**Antibody:** The antibodies were purified as follows: One volume of immune egg yolk was mixed with 9 volumes of distilled water and left overnight at  $4^{\circ}\text{C}$ . Then the supernatant was centrifuged at 4000 rpm for 10 minutes and filtered through a cheesecloth to remove any excess fat. The aqueous portion containing all the yolk protein which includes all the antibodies (IgY) was frozen and then was freeze dried.

**Animals:** Twelve Sprague Dawley rats were individually caged and supplied with free access to water. They were fed a chow which was supplemented with corn oil in order increase the fat content to 30%. Rats were divided in two groups one fed the high fat diet and the other group was fed the same diet amended with 750 mg antibody extract/kg of diet. The results after 2 week of treatment are as follows:

Days	Body weight (gr)		Total Feed Intake (gr)	
	Control	Antibody Fed	Control	Antibody Fed
Day 1	419.3	418.5		
Day 14	441.9	435.3	283.3	360.2
Difference	22.6	16.8		
gr feed needed to gain 1 gr of body weight			12.5	21.4

## Results

Feeding the antibody extract resulted in higher feed intake needed to gain 1 gram of body weight.

This result showed that using a high purity lipase (more than 20,000 U/mg protein) as antigen, produced an antibody extract that resulted in even better weight gain control than using a commercial pancreatic lipase extract (approx. 400 U) as described in the patent application.



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